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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,997	12/24/2003	Yukio Nihei	245553US0CONT	9427

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EXAMINER

WEDDINGTON, KEVIN E

ART UNIT PAPER NUMBER

1614

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/743,997

**Applicant(s)**

NIHEI ET AL.

**Examiner**

Kevin E. Weddington

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 16-28 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 29 is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-8, 10 and 12-15 is/are rejected.
- 7) ☒ Claim(s) 5, 9 and 11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12-4-03.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

RD

Claims 1-29 are presented for examination.

Applicants' information disclosure statement filed December 4, 2003 has been received and entered.

Applicants' election filed October 4, 2004 in response to the restriction requirement of September 30, 2004 has been received and entered. The applicants elected the invention described in claims 1-15 and 29 (Group I) with traverse.

Applicants' traverse of the restriction requirement is not deemed persuasive for reasons set forth in the Office action dated September 30, 2004. Therefore, the restriction requirement is hereby made Final.

Claims 16-28 are withdrawn from consideration as being drawn to the non-elected invention (37 CFR 1.142(b)).

#### ***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

#### ***Allowable Subject Matter***

Claim 29 is allowable.

#### ***Claim Objections***

Claims 5, 9 and 11 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

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with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-8, 10 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an anti-tumor composition comprising AC-7700 ((Z)-N-[2-methoxy-5-[2-(3,4,5-trimethoxyphenyl)vinyl]phenyl]-L-serinamide or salt thereof) and dexamethasone, does not reasonably provide enablement for other combinations of one or more tubulin polymerization-inhibitory active substance having anti-tumor activity and one or more anti-inflammatory active substance. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples
- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims

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The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to an anti-tumor agent (composition) comprising one or more tubulin polymerization-inhibitory active substance having ant-tumor activity and one or more anti-inflammatory active substance.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown for the other anti-tumor agent (composition) comprising one or more tubulin polymerization-inhibitory active substance having ant-tumor activity and one or more anti-inflammatory active substance.

The breadth of the claims

The claims are very broad and inclusive to all anti-tumor agent (composition) comprising one or more tubulin polymerization-inhibitory active substance having ant-tumor activity and one or more anti-inflammatory active substance.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of AC-7700 and dexamethasone.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the other anti-tumor agent (composition) comprising one or more tubulin polymerization-inhibitory active substance having ant-tumor activity and one or more anti-inflammatory active substance is effective in inhibiting

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tumor growth. The level of experimentation needed to determine the other anti-tumor agent (composition) comprising one or more tubulin polymerization-inhibitory active substance having ant-tumor activity and one or more anti-inflammatory active substance would be able to inhibit tumor growth is undue. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 1-4, 6-8, 10 and 12-15 are not allowed.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-8, 10 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pettit (5,561,122) or Cushman et al., "Synthesis and Evaluation of a Series of Benzyaniline Hydrochlorides as Potential Cytotoxic and Antimitotic Agents Acting by Inhibition of Tubulin Polymerization", J. Med. Chem, 1993, 36, pp. 2817-2821. in view of Fex et al. (3,732,260).

Pettit teaches a tubulin polymerization-inhibitory active substance, combretastatin A-4 prodrugs, same as applicants' combretastatines derivatives, are effective in treating neoplastic diseases. (See the abstract)

Cushman et al. teach various compounds, benzyaniline hydrochlorides, showed inhibition of tubulin polymerization and cytotoxicity for a wide variety of cancer cell lines. (See the abstract)

The instant invention differs from the cited reference(s) in that the cited reference(s) does or do not teach the addition of a secondary active substance, anti-inflammatory active substance, with tubulin polymerization-inhibitory active substance. However, the secondary reference, Fex et al., teaches corticoid steroid compounds such as prednisolone esters and derivatives with anti-tumor activity. Clearly, one skilled in the art would have assumed the combination of two individual anti-tumor active substances into a single composition would give an additive effect in the absence of evidence to the contrary.

The instant invention differs from the cited references in that the cited references do not teach dosage of each individual component of the anti-tumor agent (composition) as disclosed in claims 14 and 15. However, to determine a dosage range for each individual component having optimum effectiveness together to inhibit tumors is well within the level of one having ordinary skill in the art, and the skilled artisan would have been motivated to determine optimum dosages of each component to get the maximum effectiveness in the absence of evidence to the contrary.

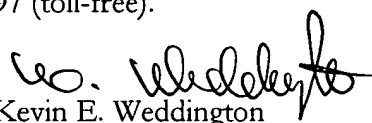
Claims 1-4, 6-8, 10 and 12-15 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Kevin E. Weddington  
Primary Examiner  
Art Unit 1614

K. Weddington  
May 15, 2005